METHOD FOR TREATING ABDOMINAL DISCOMFORT

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of provisional application Nos. 60/436,462 and 60/436,463 both filed Dec. 27, 2002, the contents of which are incorporated herein by reference in their entireties.

TECHNICAL FIELD

The present invention relates to a method for treating abdominal discomfort with a chloride channel opener, especially, a prostaglandin compound.

Further, the present invention relates to a method for treating functional gastrointestinal disorders with a chloride channel opener, especially, a prostaglandin compound.

BACKGROUND ART

Abdominal indefinite complaint or abdominal discomfort is most often experienced in our daily lives, and it includes heartburn, nausea, emesis, anorexia, epigastric pain, abdominal bloating, chronic abdominal pain, abdominal discomfort, abnormal bowel movement such as constipation and diarrhea and the like. Various disorders may cause abdominal discomfort. It is also known that abdominal discomfort may also occur as a side effect of drug, medication or surgical procedure. However, it is not yet known as to the drug that may be used for safely and effectively treating abdominal discomfort.

Patients having functional gastrointestinal disorders often report abdominal discomfort. Functional gastrointestinal disorders are characterized by chronic or recurrent gastrointestinal symptoms which are not explained by any organic, i.e. structural or biochemical, abnormality. In general, functional disorders should be distinguished from morphological or organic disorders in which the organ structures have been abnormally changed. An organic disorder may accompany functional abnormality of organs but it is surely possible to diagnose if there is any underlying organic abnormality.

Stress may effect on various organs in various ways, and the typical example of such organs is gastrointestinal tract. The interaction among stress-brain-gastrointestinal organ is called brain-gut axis, and now a days, it draws great interest of the art. In the field of clinical medicine, a group of functional disorders in which the brain-gut axis plays a central role of the pathology is called functional gastrointestinal disorders.

Typical examples of functional gastrointestinal disorders include irritable bowel syndrome (IBS) and functional dyspepsia (FD). These terms are not used for exclusively determining the nature of separate disorders but most commonly used for expressing various overlapping symptoms manifested in the upper and lower gastrointestinal tracts.

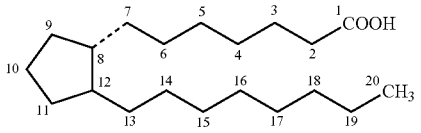
IBS is an archetype disorder of functional gastrointestinal disorders with no underlying organic abnormality. IBS patient reports continued lower gastrointestinal symptoms such as abnormal bowel movement, abdominal pain, abdominal bloating and abdominal discomfort, as well as upper gastrointestinal symptoms such as epigastric pain, hypochondriac pain, nausea, anorexia, borborygmus, vomiting, belching and heartburn.

FD patient has no underlying organic disorder such as ulcer and reports continued upper gastrointestinal tract symptoms such as abdominal pain, nausea, anorexia and slow digestion. The term "dyspepsia" means chronic or repetitious pain or discomfort mainly occurring in epigastric region. Up to 60% of the dyspepsia patients have no underlying organic disorder and are diagnosed as FD.

As explained above, functional gastrointestinal disorders are a group of disorders in which the gastrointestinal symptoms continue for a long period or by repeating a period of recrudescence and palliation without clear organic abnormalities. No systematic method has been established for treating such disorder.

Prostaglandins (hereinafter, referred to as PG(s)) are members of class of organic carboxylic acids, which are contained in tissues or organs of human or other mammals, and exhibit a wide range of physiological activity. PGs found in nature (primary PGs) generally have a prostanoic acid skeleton as shown in the formula (A):

(A)



On the other hand, some of synthetic analogues of primary PGs have modified skeletons. The primary PGs are classified to PGAs, PGBs, PGCs, PGDs, PGEs, PGFs, PGGs, PGHs, PGIs and PGJs according to the structure of the five-membered ring moiety, and further classified into the following three types by the number and position of the unsaturated bond at the carbon chain moiety:

Subscript 1: 13,14-unsaturated-15-OH

Subscript 2: 5,6- and 13,14-diunsaturated-15-OH

Subscript 3: 5,6-, 13,14-, and 17,18-triunsaturated-15-OH.

Further, the PGFs are classified, according to the configuration of the hydroxyl group at the 9-position, into α type (the hydroxyl group is an α-configuration) and β type (the hydroxyl group is a β-configuration).

PGE_1 and PGE_2 and PGE_3 are known to have vasodilation, hypotension, gastric secretion decreasing, intestinal tract movement enhancement, uterine contraction, diurectic, bronchodilation and anti ulcer activities. $PGF_{1\alpha}$, $PGF_{2\alpha}$ and $PGF_{3\alpha}$ have been known to have hypertension, vasoconstriction, intestinal tract movement enhancement, uterine contraction, lutein body atrophy and bronchoconstriction activities.

The present inventor already found that prostaglandin compounds open chloride channels, especially ClC channels, more especially ClC-2 channel (WO 03/030912, this reference is herein incorporated by reference).

However, it is not known how chloride channel openers and/or prostaglandin compounds act on abdominal discomfort, or the functional gastrointestinal disorders.

DISCLOSURE OF THE INVENTION

The present inventor has conducted intensive studies and found that a chloride channel opener, especially prostaglandin compound have a significant effect on abdominal discomfort, especially, on functional gastrointestinal disorders such as IBS and FD, which resulted in the completion of the present invention.

Namely, the present invention relates to a method for treating abdominal discomfort in a mammalian subject, which